PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-15110	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US 03/16213	International filing date *(day/month/year)* 13.06.2003	Priority date *(day/month/year)* 26.06.2002
International Patent Classification (IPC) or both national classification and IPC C07C311/08, C07D221/16, C07D235/14, C07D313/12, C07D401/06, C07D403/06, A61K31/18, A61K31/553, A61P7/10, A61P9/12		
Applicant ELI LILLY AND COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 19 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11.12.2003	28.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer English, R Telephone No. +31 70 340-2860

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/16213

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-419	as originally filed

Claims, Numbers

1-36	as originally filed
37-98	received on 27.07.2004 with letter of 27.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US 03/16213

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-36, 37,41-43,45-49(in part), 93-96, 97,98(in part)

   because:

   ☒ the said international application, or the said claims Nos. 1-36,93-96 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-36, 37, 41-43, 45-49, 97, 98 (in part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-98
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-98
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	37-92,97,98
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1-36,93-96 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2. The International Search Report was incomplete with respect to a part of the subject-matter of claims 37 (see the International Search Report for details). It was not complete for compounds of formula (I) of claim 37 in which ring C represents a phenyl group in which R1 represents halo, amino, oxo, (C_1-C_6)-alkyl, (C_1-C_6-)alkoxy, hydroxymethyl, difluoromethyl, trifluoromethyl, difluoromethoxy or trifluoromethoxy. Consequently, it is not possible to carry out a full International Preliminary Examination of claims 37 (Rule 66.1(e) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: WO 00/06137 A (Abbott Laboratories) 10 February 2000

3. **Subject-matter**

The present application concerns the use of polycyclic compounds in the treatment of disorders susceptible to steroid hormone nuclear (particularly, mineralocorticoid or glucocorticoid) receptor modulation. These compounds contain a seven-membered ring condensed with two further rings and substituted by methine group further substituted by a ring. The present application also concerns these compounds per se, subject to a number of disclaimers.

4. **Novelty**

Document D1 discloses certain tricyclic compounds which bind to the glucocorticoid receptor making them suitable for the treatment of inflammation and immune diseases. These compound consist of three phenyl groups which can be regarded as corresponding to the three rings A,B and C of the present application and a linking

group CR^1-L^1 which can be regarded as corresponding to the "-----" of the present application. However, D1 does not disclose any compounds containing a X-Y bridge linking two of the rings. Consequently, the subject-matter of claims 1-36, 37 (in so far as it is being examined, see paragraph 2 above), 38-98 appears to be new and to satisfy the requirements of Article 33(2) PCT.

5. **Inventive step**

The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses tricyclic compounds as described in paragraph above which bind to the glucocorticoid receptor. These prior-art compounds differ from those of the present application in that the former do not have the X-Y bridge present in the latter which links two of the rings.

Comparison of the pharmacological data presented in D1 (table 1) with that presented in the present application (table I) shows that the two sets of compounds have similar Ki values in the assay for glucocorticoid binding. The problem to be solved by the present claim 1 is therefore the provision of further compounds capable of modulating to steroid nuclear receptors. The applicant solves this problem by means of the polycyclic compounds of formula I as defined in claim 1.

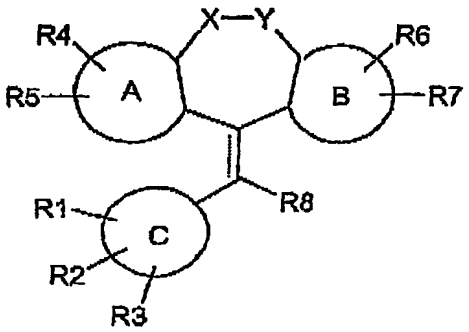
There is nothing in D1, or anywhere else in the prior art, to suggest that these compounds would modulate steroid hormone nuclear receptors. Consequently, the subject-matter of claim 1 and of all the other independent and dependent claims (in so far as it is being examined, see paragraph 2 above) can be considered to involve an inventive step and to satisfy the requirements of Article 33(3) PCT.

6. **Industrial applicability**

For the assessment of the present claims 1-36,93-98 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

R^8 represents hydrogen, halo, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl , (C_1-C_4)alkyl - (C_1-C_6)alkoxy, COR^{12} wherein R^{12} represents methoxy, ethoxy, hydroxymethyl, or methoxymethyl; (C_3-C_7)cycloalkyl, aryl or substituted aryl.

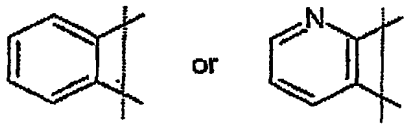
37. A novel compound of Formula I:



Formula I

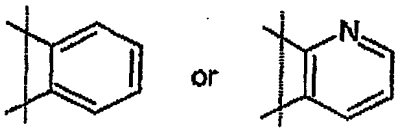
wherein,

"A" represents



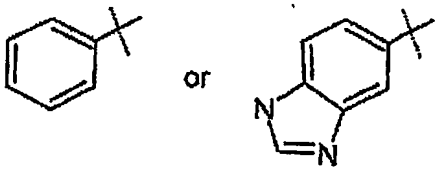
;

"B" represents



;

and "C" represents

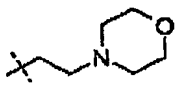
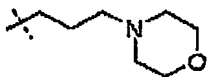


;

X and Y together represent $-CH_2-CH_2-$, $-CH_2-O-$, or $-O-CH_2-$;

"-----" represents a double bond;

R^1 represents halo, amino, oxo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxymethyl, difluromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, $SO_2NR^9R^{10}$ wherein R^9 represents (C_1-C_6)alkyl, (C_1-C_4)alkyl-(C_1-C_6)alkoxy , halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, aryl, (C_1-C_4)alkyl-aryl, heterocycle and R^{10} represents hydrogen or methyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a substituted or unsubstituted heterocycle; NH SO_2R^{11} wherein R^{11} represents amino, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy , (C_3-C_7)cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle; $NHCOR^{12}$ wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C)alkyl-(C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, NH-methylamine, NH-dimethylamine, NH-ethylamine, or heterocycle; COR^{12} wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or hydroxy(C_1-C_6)alkyl; OR^{14} wherein R^{14} represents (C_1-C)alkyl-heterocycle; or a (C_1-C_4)alkyl-heterocycle represented by the formula:


or


provided that where "C" represents an aryl group then R^1 is other than oxo.;

further provided that where "C" represents a benzo-fused heterocycle then R^1 may also represent hydrogen;

R^2 represents hydrogen, halo, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, or (C_1-C_4)alkyl-heterocycle;

R^3 represents hydrogen, halo, or (C_1-C_6)alkyl;

R^4-R^7 each independently represent hydrogen, hydroxy, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or OR^{14} wherein R^{14} represents (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, (C_1-C_4)alkyl-heterocycle, or (C_1-C_4)alkyl-(C_3-C_7)cycloalkyl ;

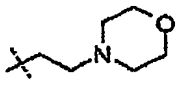
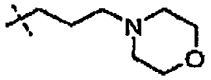
R^8 represents hydrogen, halo, (C_1-C_6)alkyl, hydroxymethyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy , or COR^{12} wherein R^{12} represents (C_1-C_6)alkoxy; (C_3-C_7)cycloalkyl, phenyl, or substituted aryl;

further provided that where C represents a phenyl ring and R^1 represents halo then at least one of R^2 and R^3 is other than hydrogen, (C_1-C_6)alkyl, aryl, substituted aryl, (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, CHF_2, or CF_3; and

further provided that where C represents a six-membered ring and R^1 represents amino or $NHCOCH_3$ and R^2 and R^3 are each hydrogen, then R^1 is not bound at the 4-position of said six-membered ring,

or a pharmaceutically acceptable salt thereof.

38. The compound according to Claim 37 wherein "C" represents a phenyl ring and R^1 represents $SO_2NR^9R^{10}$ wherein R^9 represents (C_1-C_6)alkyl, (C_1-C_4)alkyl-(C_1-C_6)alkoxy , halo(C_1-C_6)alkyl, (C_3-C_7)cycloalkyl, aryl, (C_1-C_4)alkyl-aryl, heterocycle and R^{10} represents hydrogen or methyl, or R^9 and R^{10} together with the nitrogen to which they are attached form a substituted or unsubstituted heterocycle; NH SO_2R^{11} wherein R^{11} represents amino, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, (C_1-C_6)alkoxy , (C_3-C_7)cycloalkyl, aryl, substituted aryl, heterocycle, or substituted heterocycle; $NHCOR^{12}$ wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C)alkyl-(C_1-C_6)alkoxy, balo(C_1-C_6)alkyl, NH-methylamine, NH-dimethylamine, NH-ethylamine, or heterocycle; COR^{12} wherein R^{12} represents H, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or hydroxy(C_1-C_6)alkyl; OR^{14} wherein R^{14} represents (C_1-C)alkyl-heterocycle; or a (C_1-C_4)alkyl-heterocycle represented by the formula:

 or 

or a pharmaceutically acceptable salt thereof.

39. A compound according to any one of Claims 37 and 38 wherein when R^1 represents NH SO_2R^{11}, R^{11} represents methyl, ethyl, propyl, isopropyl, butyl, or 2-methyl propyl.

40. The compound according to Claim 39 wherein R^{11} represents methyl.

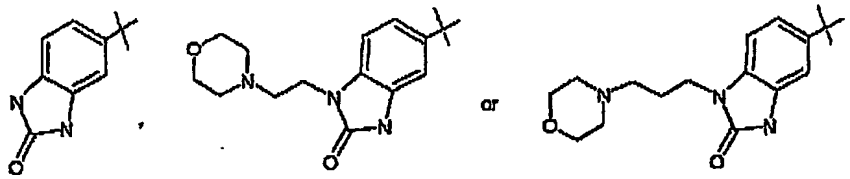
41. A compound according to any one of Claims 37 – 40 wherein R^2 represents hydrogen or (C_1-C_4)alkyl-heterocycle.

42. The compound according to Claim 41 wherein R^2 represents hydrogen.

43. A compound according to any one of Claims 37 – 42 wherein R^3 represents hydrogen.

44. A compound according to any one of claims 37, 41-43 wherein "C" represents a benzofused heterocycle having a non-hydrogen substituent at at least one of

R1-R3, wherein said benzofused heterocycle having a non-hydrogen substituent is given by the following:



45. A compound according to any one of Claims 37-44 wherein R^4 and R^6 each independently represent hydrogen, halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, or OR^{14} wherein R^{14} represents (C_1-C_4)alkyl-aryl, (C_1-C_4)alkyl-substituted aryl, (C_1-C_4)alkyl-heterocycle, or (C_1-C_4)alkyl-(C_3-C_7)cycloalkyl.

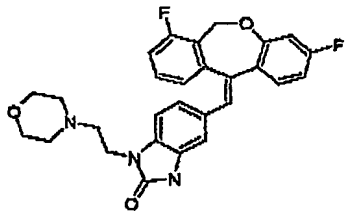
46. A compound according to any one of Claim 37- 45 wherein R^5 and R^7 each independently represent hydrogen, hydroxy, halo, (C_1-C_6)alkyl, or (C_1-C_6)alkoxy.

47. A compound according to any one of Claims 37-46 wherein R^8 represents hydrogen, halo, (C_1-C_6)alkyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy , or (C_3-C_7)cycloalkyl.

48. The compound according to Claim 47 wherein R^8 represents halo (C_1-C_6)alkyl, (C_1-C_4)alkyl -(C_1-C_6)alkoxy.

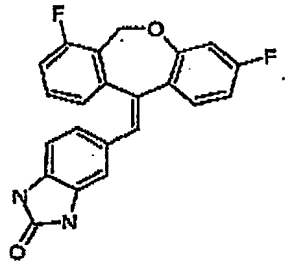
49. The compound according to Claim 47 wherein R^8 represents hydrogen.

50. A compound of the formula



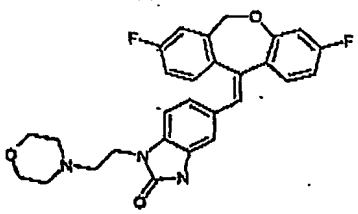
or a pharmaceutically acceptable salt thereof.

51. A compound of the formula



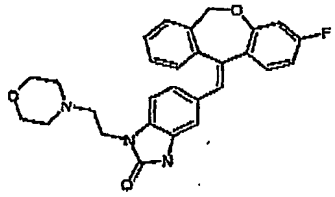
or a pharmaceutically acceptable salt thereof.

52. A compound of the formula



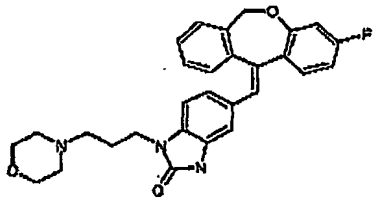
or a pharmaceutically acceptable salt thereof.

53. A compound of the formula



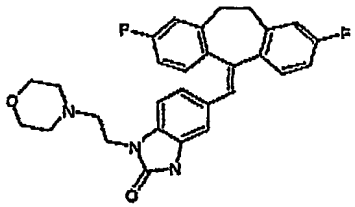
or a pharmaceutically acceptable salt thereof.

54. A compound of the formula



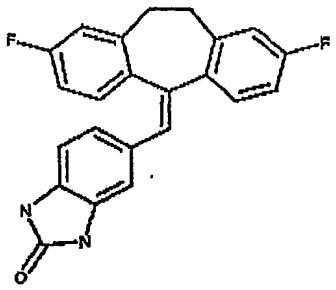
or a pharmaceutically acceptable salt thereof.

55. A compound of the formula



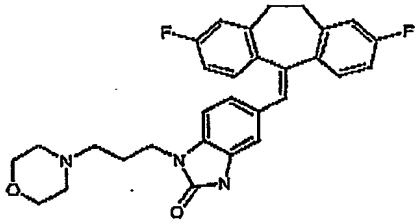
or a pharmaceutically acceptable salt thereof.

56. A compound of the formula



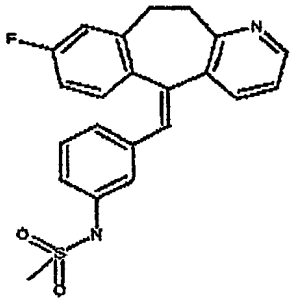
or a pharmaceutically acceptable salt thereof.

57. A compound of the formula



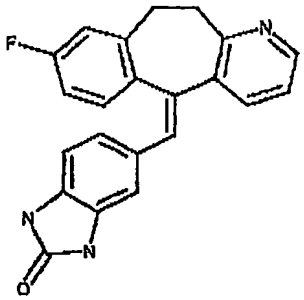
or a pharmaceutically acceptable salt thereof.

58. A compound of the formula



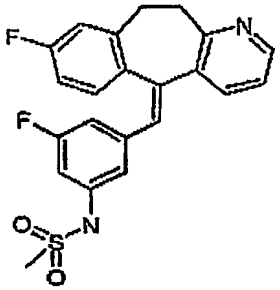
or a pharmaceutically acceptable salt thereof.

59. A compound of the formula



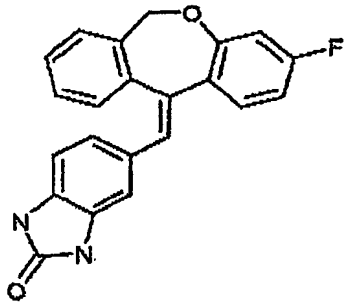
or a pharmaceutically acceptable salt thereof.

60. A compound of the formula



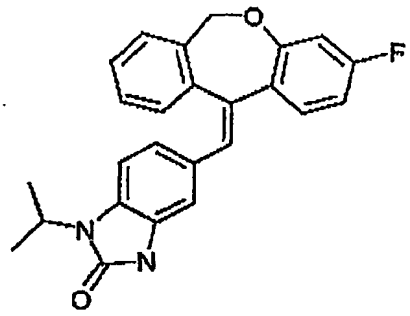
or a pharmaceutically acceptable salt thereof.

61. A compound of the formula



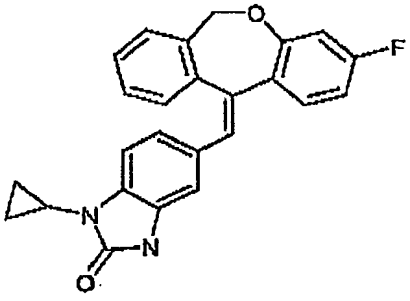
or a pharmaceutically acceptable salt thereof.

62. A compound of the formula



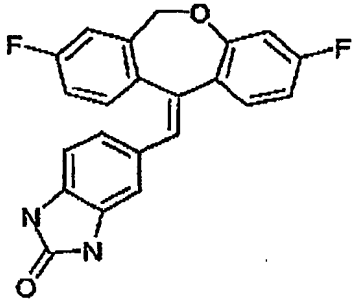
or a pharmaceutically acceptable salt thereof.

63. A compound of the formula



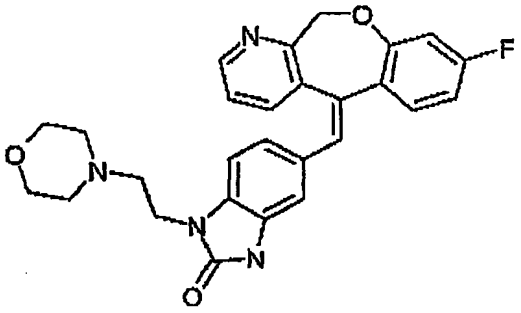
or a pharmaceutically acceptable salt thereof.

64. A compound of the formula



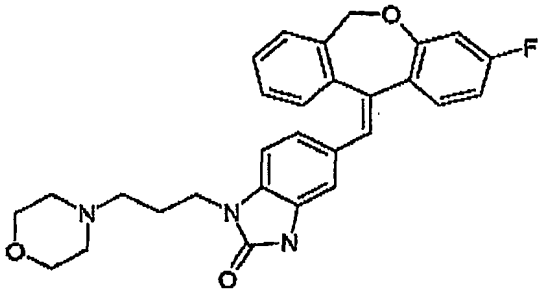
or a pharmaceutically acceptable salt thereof.

65. A compound of the formula



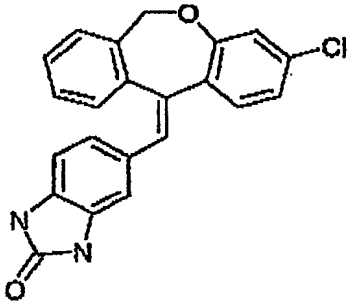
or a pharmaceutically acceptable salt thereof.

66. A compound of the formula



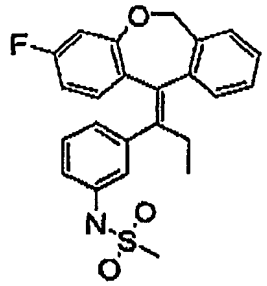
or a pharmaceutically acceptable salt thereof.

67. A compound of the formula



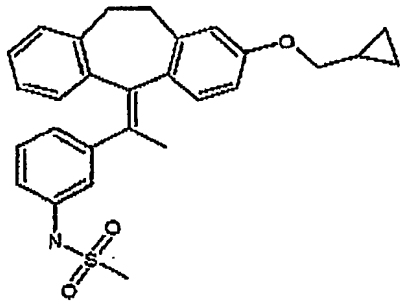
or a pharmaceutically acceptable salt thereof.

68. A compound of the formula



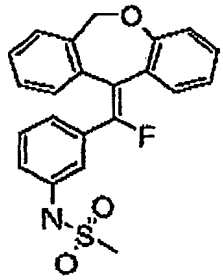
or a pharmaceutically acceptable salt thereof.

69. A compound of the formula



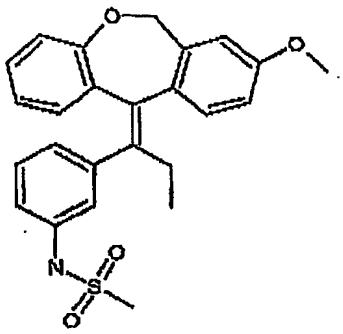
or a pharmaceutically acceptable salt thereof.

70. A compound of the formula



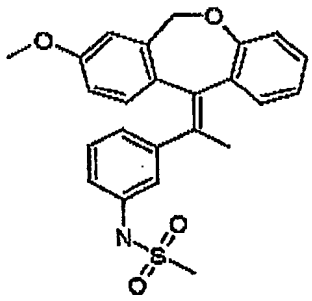
or a pharmaceutically acceptable salt thereof.

71. A compound of the formula



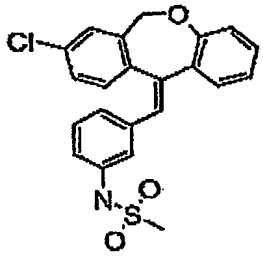
or a pharmaceutically acceptable salt thereof.

72. A compound of the formula



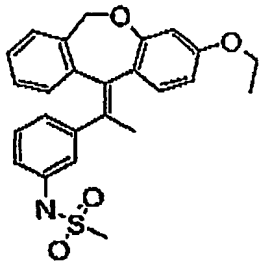
or a pharmaceutically acceptable salt thereof.

73. A compound of the formula



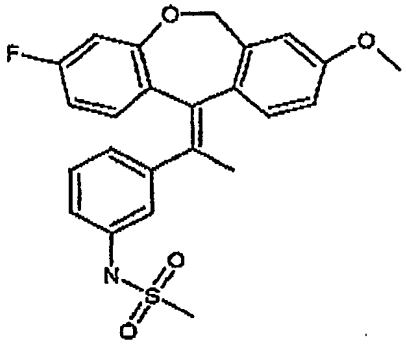
or a pharmaceutically acceptable salt thereof.

74. A compound of the formula



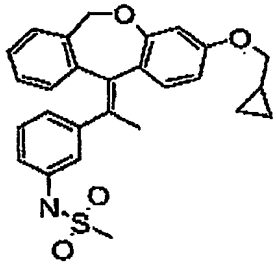
or a pharmaceutically acceptable salt thereof.

75. A compound of the formula



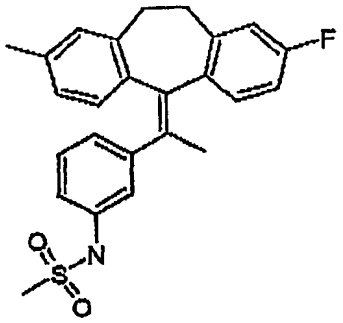
or a pharmaceutically acceptable salt thereof.

76. A compound of the formula



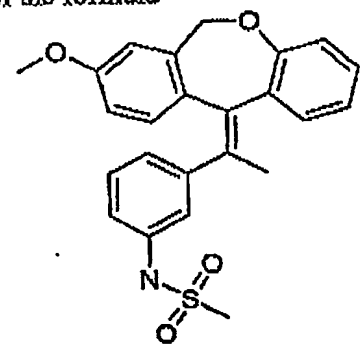
or a pharmaceutically acceptable salt thereof.

77. A compound of the formula



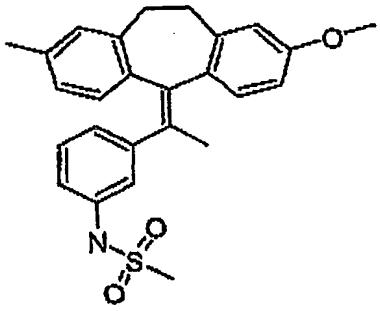
or a pharmaceutically acceptable salt thereof.

78. A compound of the formula



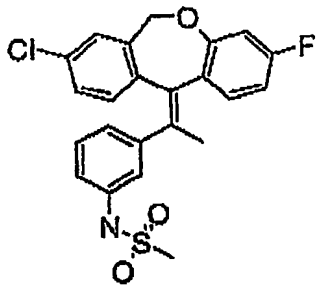
or a pharmaceutically acceptable salt thereof.

79. A compound of the formula



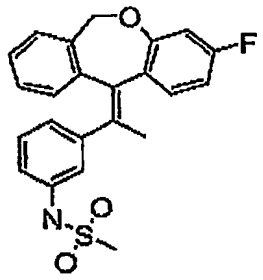
or a pharmaceutically acceptable salt thereof.

80. A compound of the formula



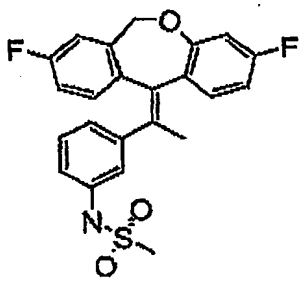
or a pharmaceutically acceptable salt thereof.

81. A compound of the formula



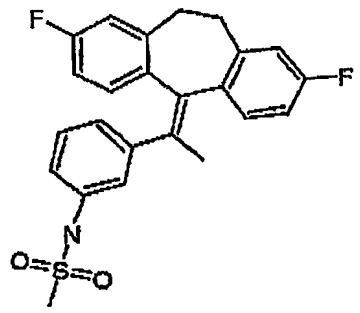
or a pharmaceutically acceptable salt thereof.

82. A compound of the formula



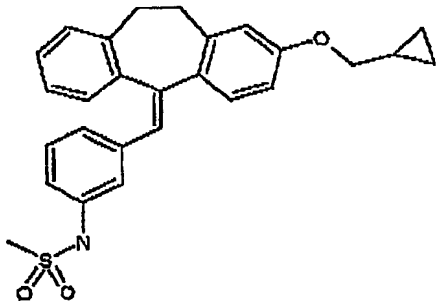
or a pharmaceutically acceptable salt thereof.

83. A compound of the formula



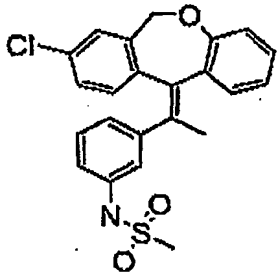
or a pharmaceutically acceptable salt thereof.

84. A compound of the formula



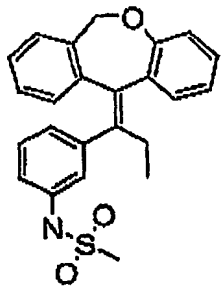
or a pharmaceutically acceptable salt thereof.

85. A compound of the formula



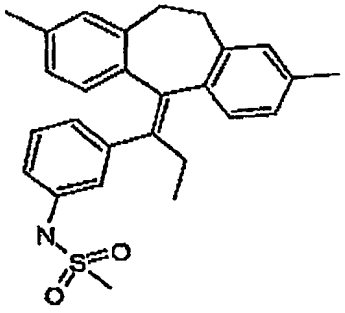
or a pharmaceutically acceptable salt thereof.

86. A compound of the formula



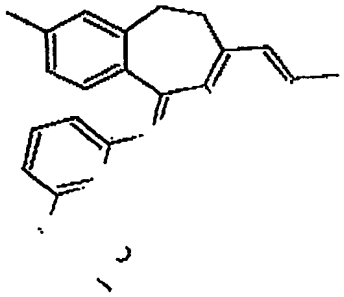
or a pharmaceutically acceptable salt thereof.

87. A compound of the formula



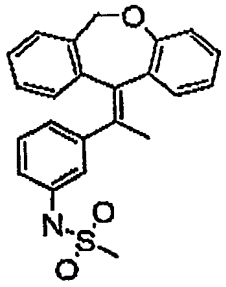
or a pharmaceutically acceptable salt thereof.

88. A compound of the formula



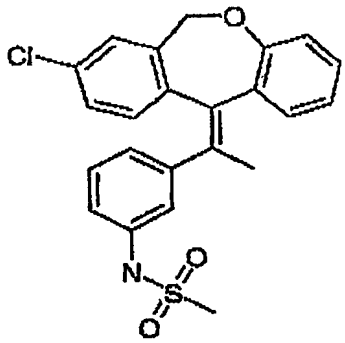
or a pharmaceutically a[redacted]ic salt thereof.

89. A [redacted]pound of the formula



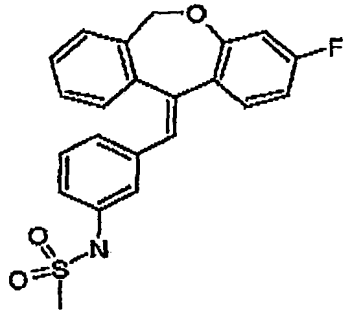
or a pharmaceutically acceptable salt thereof.

90. A compound of the formula



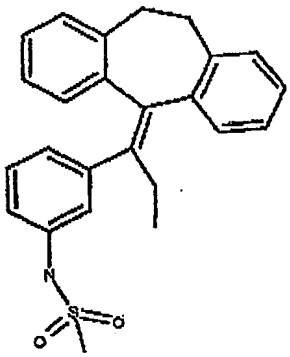
or a pharmaceutically acceptable salt thereof.

91. A compound of the formula



or a pharmaceutically acceptable salt thereof.

92. A compound of the formula



or a pharmaceutically acceptable salt thereof.

93. A method of treating a physiological disorder susceptible to mineralocorticoid or glucocorticoid receptor modulation wherein said disorder is selected from the group consisting of Conn's Syndrome, primary and secondary hyperaldosteronism, increased sodium retention, increased magnesium and potassium excretion (diuresis), increased water retention, hypertension (isolated systolic and combined systolic/diastolic), arrhythmias, myocardial fibrosis, myocardial infarction, Bartter's Syndrome, disorders associated with excess catecholamine levels, diastolic and systolic congestive heart failure (CHF), psychoses, cognitive disorders, memory disturbances, depression, bipolar disorder, anxiety disorders, personality disorders, breast cancer, peripheral vascular disease, diabetic nephropathy, cirrhosis with edema and ascites, esophageal varicies, Addison's Disease, muscle weakness, increased melanin pigmentation of the skin, weight loss, hypotension, hypoglycemia, Cushing's Syndrome, obesity, hypertension, glucose intolerance, hyperglycemia, diabetes mellitus, osteoporosis, polyuria, polydipsia, inflammation, autoimmune disorders, tissue rejection associated with organ transplant, malignancies such as leukemias and lymphomas, acute adrenal insufficiency, congenital adrenal hyperplasia, rheumatic fever, polyarteritis nodosa, granulomatous polyarteritis, inhibition of myeloid cell lines, immune proliferation/apoptosis, HPA axis suppression and regulation, hypercortisolemia, modulation of the Th1/Th2 cytokine balance, chronic kidney disease, stroke and spinal cord injury, hypercalcemia, hypergylcemia, acute adrenal insufficiency, chronic primary adrenal insufficiency, secondary adrenal insufficiency, congenital adrenal hyperplasia, cerebral edema, thrombocytopenia, and Little's syndrome, systemic inflammation, inflammatory bowel disease, systemic lupus erythematosus, discoid lupus erythematosus, polyartitis nodosa, Wegener's granulomatosis, giant cell arthritis, rheumatoid arthritis, osteoarthritis, hay fever, allergic rhinitis, contact dermatitis, atopic dermatitis, exfoliative

dermatitis, urticaria, angioneurotic edema, chronic obstructive pulmonary disease, asthma, tendonitis, bursitis, Crohn's disease, ulcerative colitis, autoimmune chronic active hepatitis, hepatitis, cirrhosis, inflammatory scalp alopecia, panniculitis, psoriasis, inflamed cysts, pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, dermatomyositis, eosinophilic fasciitis, relapsing polychondritis, inflammatory vasculitis, sarcoidosis, Sweet's disease, type 1 reactive leprosy, capillary hemangiomas, lichen planus, , erythema nodosum, acne, hirsutism, toxic epidermal necrolysis, erythema multiform, cutaneous T-cell lymphoma, emphysema, Alzheimer's Disease, and multiple sclerosis., comprising administering to a patient in need thereof an effective amount of a novel compound of Formula I according to claim 37.

94. The method according to claim 93, wherein said disorder is diastolic or systolic congestive heart failure, inflammation, rheumatoid arthritis, an autoimmune disorder, asthma, or chronic obstructive pulmonary disease

95. The method according to claim 94, wherein said disorder is diastolic or systolic congestive heart failure or rheumatoid arthritis.

96. A method of modulating a steroid hormone nuclear receptor , wherein said steroid nuclear receptor is the mineralocorticoid receptor or the glucocorticoid receptor , comprising administering to a patient in need thereof an effective amount of a compound of Formula I according to Claim 37.

97. A pharmaceutical composition comprising an effective amount of a compound of Formula I according to Claim 37 in combination with a pharmaceutically acceptable carrier.

98. The use of a compound of Formula I according to Claim 37 for the manufacture of a medicament for the treatment of diastolic or systolic congestive heart failure or rheumatoid arthritis.